

**REMARKS**

Reconsideration is requested.

Claim 17 has been canceled, without prejudice. Claims 1-16 and 18 are pending.

The specification has been amended to include the new pages 12-15, attached. Also attached is a marked-up copy of the amended pages indicating the changes made in underlined handwritten text. Specifically, the specification has been amended to include sequence identifiers, as required by the Examiner in the paragraph spanning pages 2-3 of the Office Action dated November 25, 2002 (Paper No. 9).

Claim 17 has been canceled, without prejudice, to advance prosecution. Cancellation of claim 17 makes the Section 101 rejection of the same moot.

Withdrawal of the Rule 75(c) objection of claims 14-16 noted in paragraph 3 on page 3 of Paper No. 9 is requested along with examination of claims 4-16.

The Section 112, second paragraph, rejection of claims 1-3 is obviated by the above amendments. The claims are submitted to be definite.

The Section 103 rejection of claims 1-3 over Gibson (Genome Research (1996) 6:995-1001) in view of WalkerPeach (U.S. Patent No. 6,395,470), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments as well as the attached Declaration of Dr. Malnati.

The applicants submit that, with regard to Gibson et al., the GC content of target sequence is not a valid criterion to design functional TaqMan probes (Gibson et al. page 995, left-hand column, lines 17-20). The enclosed Declaration under Rule 132 shows that probe sequences designed in accordance with Gibson et al., i.e., maintaining the

same G+C content and the same sequence length as the target nucleic acid (HHV6, see Examples 1 and 2 of the present application), does not allow for target DNA quantification, in contrast to the Calibrator designed in accordance with the presently claimed invention. This is due to the differences of T<sub>m</sub> observed between the control sequences (G+C 1 and 2) and either the Calibrator or the primers, which do not allow the control sequences to satisfy the TaqMan probe requirements, for the reasons explained in the Declaration.

In addition, the combination of Gibson et al with WalkerPeach is submitted, with due respect, to be improper since the control ("calibrator") described by WalkerPeach is used for techniques such as Real time PCR, NASBA and TMA, but not for nucleic acid quantification by means of 5' nuclease assays, as in the present invention (see claim 1, step (c)). The characteristics of control sequences for these applications are completely different from those required for 5' nuclease assay - the latter are specifically described in other patents, such as U.S. Patent No. 5,210,015 (Gelfand DH et al., cited on page 2, lines 11-12 of the present application, identified in the attached Declaration as "US 520015", copy attached). A copy of U.S. Patent No. 5,876,930 referred to in the attached Declaration is also attached. Therefore the ordinarily skilled person would not have looked at WalkerPeach in an attempt to find a valid internal control for use in a modified TaqMan technique according to the claimed invention.

Reconsideration and withdrawal of the Section 103 rejection of claims 1-3 are requested.

In view of the above and attached, the claims are submitted to be in condition for allowance and a Notice to that effect is requested.


**LOCATELLI et al.**  
Serial No. **09/831,820**  
April 25, 2003

The Examiner has requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



B. J. Sadoff  
Reg. No. 36,663

BJS:plb  
1100 North Glebe Road, 8th Floor  
Arlington, VA 22201-4714  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100